

Investigation the correlation between methylation patterns of DNMT1 gene promoter with Ecad gene expression in patients with Acute Myeloid Leukemia (M3)

Abstract

Aim: Acute promyelocytic leukemia (APL) is one of the subtype of Acute Myeloid leukemia (AML) in which a fusion protein has a negative impact on differentiation of the myeloid progenitor cells and their maturation would stay at promyelocytic stage. DNA methylation is an epigenetic mechanism that often modifies the function of genes and affect gene expression, which may sometimes lead to cancer development. Many studies have found that DNA methylation could predict clinical outcome in AML patients and abberant DNA methylation can serves as a biomarker for risk stratification. The key role of DNMT1 in pathogenesis of various cancers and control of methylation motivated us to have study in this field. Ecad gene is also a tumor suppresor gene and play a pivotal role in controlling the proliferation of mammalian cells. One of the factors controlling its expression is promoter methylation by DNMT1 enzymes. Consequently, investigatong the correlation between DNMT1 promoter methylation and Ecad gene expression would be of significance in producing new drugs for treating APL disease.

Methods: The DNA of white blood cells of 15 patients and 5 healthy control subjects were extracted, treated with bisulfite, and DNMT1 gene promoter methylation was subsequently analyzed using the MSP technique. We used Real-time PCR to measure the expression level of Ecad gene to find out if there is any relation between pattern of DNMT1 gene promoter methylation and Ecad gene expression.

Results: After performing MSP, we found that the promoter methylation pattern of DNMT1 was unmethylated. Unmethylation of DNMT1 gene promoter was detected in 100% of samples. Ecad expression was upregulated 3.1 fold compared to control group.

Conclusion and discussion: As DNMT1 gene promoter was unmethylated and it was upregulated in comparison to controls, using epigenetic mechanisms for reducing it's expression would be of help; however, MSP may not disclose subtle changes in methylation level. Analyzing Ecad expression, we found that there is not obvious correlation between methylation pattern of DNMT1 gene and Ecad expression in patients with APL.

Key words: Acute promyelocytic leukemia, promoter methylation, Ecad, DNMT1